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2245 '99 SEP 13 A9:37

SEP 10 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Docket No. 99D-0193
Proposed Rule: Supplements and Other Changes to an Approved Application

Dear Sir/Madam:

Reference is made to the above-noted Proposed Rule originally published in the Federal Register on 28 June 1999, Docket Number 99D-0193.

At this time, on behalf of The R.W. Johnson Pharmaceutical Research Institute (RWJPRI), we wish to provide our comments to this Draft Guidance. Our comments are both General and specific and are identified as such.

We greatly appreciate the opportunity to comment on this document and look forward to similar opportunities in the future.

Very truly yours,

Donna Panasewicz
Director
Regulatory Affairs

Attachment

99N-0193

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General Comments

We concur with PhRMA's and PDA's recommendations that the term "validate" used throughout the document should be revised to "assess", "evaluate" or "confirm", to avoid potential confusion with the cGMP definition of "validation" which would not apply here.

We also concur with PhRMA's opinion regarding the fact that the proposed changes do not meet the intent of Congress and FDAMA regarding the fact that what was being hoped to be achieved was the reduction in prior approval supplements and reporting requirements which in fact will not be met by the changes to the proposed rule.

We respectfully request that the Agency consider some sort of "Grandfathering" of changes which are already in progress by industry based upon already approved SUPAC guidances. There are many cases where regulatory filing strategies have already been implemented internally in industry and now with the change to 314.70 the reporting requirements have changed., ie. from a CBE 30 to a PAS, or there was no reporting requirement in the current 314.70 and now one exists. Our ability to continue to supply product to the marketplace can be adversely impacted by now having to redefine the reporting requirements and extend the time to implementation.

Finally, it is our opinion that the Agency should reassess and remove the submission requirements contained in these proposed rules specific to cGMP's, ie., SOP's and validation reports. To require industry to submit these type of documents could result in conflicts between Agency Headquarters and the Agency District Offices and represents an increased burden on industry.

Specific Comments

314.70 (a)(6) – listing all CM&C changes in a cover letter to a supplement or annual report

We agree that a summary of the content should be included in the cover letter for a supplement, however we disagree that a list of all changes contained in the annual report be included in a cover letter.
The annual report is accompanied by Form FDA2252. The form has a section which requests identification of type of information and in which section it is located. The form clearly identifies the purpose of the communication. To restate what is already contained in the CM&C section in a cover letter would be redundant. We ask that the agency consider modifying/expanding Form FDA 2252 to include the number of volumes in each section which would help the Agency ascertain how many volumes are part of the annual report and in which volume specific sections are contained.

314.70(d)(3) an applicant must submit in the annual report a list of all products involved and:
(3)(iii) the date each change was made, a cross reference to relevant validation protocols and/or SOP's, and relevant data from studies and test performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as these factors may relate to the safety or effectiveness of the product (validation).
It should not be necessary to provide cross-reference to relevant validation protocols and/or SOP's. The SOP's are not normally filed with the FDA. Secondly, the companies have to make a statement that the effects of the changes have been validated, and thirdly, stability data and other relevant data must be submitted. The onus is on the company to have the relevant information available at the time of an Agency inspection. To provide the suggested cross-reference information is adding an unnecessary burden on a company which has no practical or useful use.

314.70(d)(2)(i)
Any changes made to comply with an official compendium that is consistent with FDA requirements and provides increased assurance that the drug will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess.
Changes made to comply with changes in an official compendium should not have to include all the information needed for non-compendial products. A full description of the test methods and limits should not be necessary. Furthermore, the company should not have to submit data demonstrating the suitability of a compendial change for the drug product if the compendial change is for a test method change or other change not specifically affecting the quality or the morphology of the material in question.

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